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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/520,760	03/07/2000	Krishan L. Taneja	BP9806US-CP1	9118
23544	7590	01/08/2004	EXAMINER	
BRIAN D. GILDEA APPLIED BIOSYSTEMS 15 DEANGELO DRIVE BEDFORD, MA 01730			SITTON, JEHANNE SOUAYA	
			ART UNIT	PAPER NUMBER
			1634	

DATE MAILED: 01/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

S.M.

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Office Action Summary	Application No.	Applicant(s)	
	09/520,760	TANEJA, KRISHAN L.	
	Examiner	Art Unit	
	Jehanne Souaya Sitton	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 09 October 2003.
- 2a) This action is **FINAL**. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1,2,10-12,29,31,33,34,38-40,45,47,49,50,54-56,64,65 and 78-80 is/are pending in the application.
- 4a) Of the above claim(s) See Continuation Sheet is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 10 and 11 is/are rejected.
- 7) Claim(s) 12 is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) The translation of the foreign language provisional application has been received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) 10/2003.
- 4) Interview Summary (PTO-413) Paper No(s). _____.
- 5) Notice of Informal Patent Application (PTO-152)
- 6) Other: _____

Continuation of Disposition of Claims: Claims withdrawn from consideration are 1,2,29,31,33,34,38-40,45,47,49,50,54-56,64,65 and 78-80.

DETAILED ACTION

1. Currently, claims 1, 2, 10-12, 29, 31, 33, 34, 38-40, 45, 47, 49, 50, 54-56, 64-65, and 78-80 are pending in the instant application. Claims 1, 2, 29, 31, 33, 34, 38-40, 45, 47, 49, 50, 54-56, 64-65, and 78-80 have been withdrawn from consideration as being drawn to non elected inventions, and claims 10-12, as elected (see office action mailed 4/21/2003, section 1), are under consideration at this time. It is noted that the claims under consideration have not been amended to reflect the election and are drawn to probe compositions that have not been elected, searched, or considered. All the amendments and arguments have been thoroughly reviewed but are deemed insufficient to place this application in condition for allowance. Any rejections not reiterated are hereby withdrawn. The following rejections are maintained from the previous office action, with regard to the amended claims, however as the claims have been amended, *cp 104* such rejections^{also} contain new grounds of rejection, necessitated by amendment. These rejections are placed under the heading "New Grounds of Rejection". They constitute the complete set being presently applied to the instant Application. Response to Applicant's arguments follow.

This action is FINAL.

Claim Objections

2. Claim 12 is objected to for being dependent on a rejected claim.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

4. Claims 10-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a probe set comprising PNA probes with the specific PNA formula set forth in the claims in the consisting of nucleobases of SEQ ID NOS 1-118, does not reasonably provide enablement for A) a probe set comprising PNA probes of 10-30 subunits with the specific PNA formula set forth in the claims but with any nucleobase portion suitable for identifying, or enumerating human chromosomes X, Y, 1-3, 6, 8, 10-12, and 16-18 or B) the probe set of A comprising PNA probes with the specific PNA formula set forth in the claims but “comprising” a probing nucleobase sequence at least a portion of which is at least ninety percent homologous to the nucleobase sequence or their complements of SEQ ID NOS 1-118. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims encompass a probe set comprising PNA probes with the specific PNA formula set forth in the claims but with as little as 10 subunits and up to 30 subunits and any nucleobase portion suitable for identifying, or enumerating human chromosomes X, Y, 1-3, 6, 8, 10-12, and 16-18 or said probe set comprising PNA probes with the specific PNA formula set forth in the claims but “comprising” a probing nucleobase sequence at least a portion of which is at least ninety percent homologous to the nucleobase sequence or their complements of SEQ ID NOS 1-118.

The specification teaches the specific constructs of table 2 with the specific nucleobase containing portions outlined in the specification, that is “consisting” of SEQ ID NOS 1-118. The

specification demonstrates the use of such as probes as chromosome specific probes. However, the claims are of a much broader scope, such that the specification does not enable the skilled artisan to predictably make or use the claimed products in methods of detecting, identifying, or enumerating specific chromosomes.

The specification teaches that the nucleobase sequence of the non nucleic acid probes is the sequence recognition portion of the construct. Probes encompassed by all of the claims include for example, PNA probes of 10-30 subunits. While the specific probes of table 2 have been shown to be specific for identifying a chromosome, it is unpredictable as to whether altered nucleobase containing PNA probes which can comprise minimally “any” 10 to as many as 30 subunits (amended claim 10), or wherein the 10-30 subunits comprise a probing nucleobase sequence at least a portion of which is only “at least” 90% homologous to the recited SEQ ID NOS: (amended claim 11) would be specific for identifying a chromosome. With regard to probes having as little as 10 or even 11 or 15 subunits, etc with any nucleobase composition, or a specific nucleobase composition, including PNAs, it is unpredictable as to whether such a sequence would be specific for a particular chromosome and therefore be capable of identifying, enumerating, or detecting any specific chromosome, including those set forth in the claims. A 10 mer sequence, or even 11, or 15 mers, etc, would be expected to appear numerous times throughout the genome, thus identifying a variety of nucleic acid sequences that are not specific for a particular chromosome. Given that there are 3000 billion nucleotides in the human genome, one would statistically expect a 10 mer, for example, to occur every million nucleotides. This results in any particular 10 mer nucleobase portion occurring 3000 times in genomic sequences. However, the specification has provided no guidance as to which specific nucleobase

portion, other than those designated by SEQ ID NO, would be capable of exhibiting specificity for a particular chromosome. While the skilled artisan would be able to envision some constructs that would seemingly be specific for a particular chromosome using sequence comparison with the known sequences in Genbank, the specification teaches that in functional assays, “many of the sequences originally chosen did not prove to be highly specific despite alignment analysis indications that they should be specific to the chromosome sought to be detected” (see p. 25, lines 2-4). Therefore, the specification teaches of the unpredictability in designing chromosome specific probes. Given such teachings, the skilled artisan would not be able to predictably determine the identity of the probing nucleobase containing portions of the probes encompassed by claims 10 and 11 which would be able to function in identifying, detecting, or enumerating human chromosomes X, Y, 1-3, 6, 8, 10-12, and 16-18 in a sample, other than by specific SEQ ID NO.

Claim 10 encompasses products with no specifically defined nucleobase structure, and such products, while being able to detect a certain chromosome would not necessarily be specific for detecting chromosome X, for example. Probes of 10-30 subunits “comprising” a probing nucleobase sequence where only a portion are at least 90% homologous to the nucleobase sequence of SEQ ID NO 1 (claim 11) encompasses a probe with altered nucleobase containing portions, wherein it is unpredictable as to whether such a probe would be able to be used to detect chromosome X, for example. Claim 10 necessarily encompasses such sequences as claim 11 is dependent from claim 10. However, due to the lack of guidance from the specification and the unpredictability taught in the specification with regard to constructing probes which can be used to identify a *specific* chromosome based even on already known nucleic acid sequences

from chromosomes, undue experimentation would be required of the skilled artisan to make and use the extremely large number of different molecules encompassed by the broad scope of the claimed invention. A large amount of unpredictable trial and error analysis would be required for the skilled artisan to make and use probes as encompassed by the claims. Such experimentation is considered undue.

Response to Arguments

The response asserts that the claims have been amended to define PNA probes of a defined length and a defined structure. This amendment was not sufficient to overcome the rejections, however, because amended claims 10-11 still encompass probes with undefined or only partially defined nucleobase structures. As the nucleobase structure is what imparts the use of the probes for identifying a *specific* chromosome, the claims still encompass a large number of PNA probes which are not predictably capable of detecting a specific chromosome. As the specification has not defined what part of the of the nucleobase containing portion imparts such specificity, other than the full nucleobase containing portion set forth in the sequence identifiers, or which nucleobases can be altered (deleted, added, changed) and still impart such specificity to the probe, a large amount of unpredictable trial and error analysis would be required to make and use the broad scope of the encompassed PNA probes. The amendment to the claims has been sufficient to overcome the rejection with regard to claim 12 as this claim is drawn to a probe set comprising 118 PNA probes with the PNA formula set forth in the claims wherein the probing nucleobase sequence for each probe is the sequence of each SEQ ID NO.

5. Claims 10-11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims broadly encompass a probe set comprising PNA probes with the specific PNA formula set forth in the claims but with as little as 10 subunits and up to 30 subunits and any nucleobase portion suitable for identifying, or enumerating human chromosomes X, Y, 1-3, 6, 8, 10-12, and 16-18 or said probe set comprising PNA probes with the specific PNA formula set forth in the claims but “comprising” a probing nucleobase sequence at least a portion of which is at least ninety percent homologous to the nucleobase sequence or their complements of SEQ ID NOS 1-118.

The specification teaches that a use for the probes of the claimed invention are for improving the specificity, sensitivity and reliability of probe based assays for the detection of chromosomes X, Y, 1-3, 6, 8, 10-12, and 16-18. The specification teaches the specific constructs of table 2 with the specific nucleobase containing portions outlined in the specification, that is “consisting” of SEQ ID NOS 1-118. The specification demonstrates the use of such probes as chromosome specific probes. The specification teaches that the nucleobase sequence of the non nucleic acid probes is the sequence recognition portion of the construct. While the specific probes of table 2 have been shown to function as specific for identifying a particular chromosome, the specification does not teach of a predictable structure/function correlation between PNA probes which are minimally 10 and up to 30 subunits with “any” nucleobase containing portion (encompassed by amended claim 10) or wherein the 10-30 subunits comprise

a probing nucleobase sequence at least a portion of which is only “at least” 90% homologous to the recited SEQ ID NOS: (amended claim 11) would be specific for identifying a chromosome. With regard to probes having as little as 10 or even 11 or 15 subunits, etc with any nucleobase composition, or a specific nucleobase composition, including PNAs, the specification does not teach whether any such sequence would be specific for a particular chromosome and therefore be capable of identifying, enumerating, or detecting any specific chromosome, including those set forth in the claims. A 10 mer sequence, or even 11, or 15 mers, etc, would be expected to appear numerous times throughout the genome, thus identifying a variety of nucleic acid sequences that are not specific for a particular chromosome. Given that there are 3000 billion nucleotides in the human genome, one would statistically expect a 10 mer, for example, to occur every million nucleotides. This results in any particular 10 mer nucleobase portion occurring 3000 times in genomic sequences. However, the specification has provided no guidance as to which specific nucleobase portion, other than those designated by SEQ ID NO, would be capable of exhibiting specificity for a particular chromosome. While the skilled artisan would be able to envision some constructs that would seemingly be specific for a particular chromosome using sequence comparison with the sequences in Genbank, the specification teaches that in functional assays, “many of the sequences originally chosen did not prove to be highly specific despite alignment analysis indications that they should be specific to the chromosome sought to be detected” (see p. 25, lines 2-4). Therefore, the specification teaches of the unpredictability in designing chromosome specific probes. Given such teachings, the skilled artisan would not be able to predictably envision the detailed nucleobase containing portions of the probes encompassed by claims 10 and 11 which would be able to function in identifying, detecting, or enumerating

human chromosomes X, Y, 1-3, 6, 8, 10-12, and 16-18 in a sample, other than by specific SEQ ID NO.

Further, amended claim 10, for example, is drawn to probes with no specifically defined probing nucleobase sequences with as little as 10, 11, 15, etc subunits, and claim 11 is drawn to probes with only a partially defined probing nucleobase sequences. Probes encompassed by these claims include probing nucleobase sequences from any part of the genome, including millions of sequences some of which were undefined at the time the specification was filed. However, the probes with sequences outlined in table 2 are not representative of the millions of sequences encompassed by the claims.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

Response to Arguments

The response asserts that claim 10 has been amended to define the PNA structure and that the methods disclosed in the specification for generating sequences suitable for chromosome determination using PNA probes fully support the scope of the presently claimed subject matter. This argument has been thoroughly reviewed but was found unpersuasive because the amendment to claim 10 has not further defined the nucleobase containing portion of the probe which the specification teaches is the sequence recognition portion of the construct. As amended

claim 10 is still drawn to probes with no specifically defined probing nucleobase sequences, although the PNAs now have a length limitation with regard to number of subunits, and amended claim 11 is drawn to probes with only a partially defined probing nucleobase sequences, probes encompassed by these claims include probing nucleobase sequences from any part of the genome, including millions of sequences some of which were undefined at the time the specification was filed. However, the probes with sequences outlined in table 2 are not representative of the millions of sequences encompassed by the claims. In addition, the specification provides no demonstration of possession of a set of PNA probes, with 10, or 11, or 15, etc, subunits that are specific for any chromosome or capable of identifying, enumerating, or detecting a specific chromosome or chromosomes. As such, the claims remain rejected under 35 USC 112/first paragraph. The amendment to the claims has been sufficient to overcome the rejection with regard to claim 12 as this claim is drawn to a probe set comprising 118 PNA probes with the PNA formula set forth in the claims wherein the probing nucleobase sequence for each probe is the sequence of each SEQ ID NO.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

- (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
- (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claim 10 is rejected under 35 U.S.C. 102(e) and 102(a) as being anticipated by Hyldig-Nielsen et al (US Patent 5,985,563, 102(a) date: 11/16/1999; 102(e) date: 5/18/1995).

It is noted that the instant case claims priority from application 09/7363,632. The instant *90 1104* claims have been awarded an effective filing date of the 3/7/2000 as the '632 application did not teach or suggest non nucleic acid probes to chromosome 3, 11, or 12.

Amended claim 10 is drawn to a probe set comprising at least 13 non nucleic acid probes wherein no nucleobase portions are defined. Hyldig-Nielsen teaches a set of at least 13 PNA probes of 10-30 subunits in length with a nucleobase containing portion as set forth in table 4. It is noted that the amended recitation of "which is suitable for detecting, identifying or enumerating chromosomes X, Y, 1-3, 6, 8, 10-12, 16, 17, and/or 18" is considered an intended use, and has been given no patentable weight. However, even if such was given weight, as chromosomes X, Y, 1-3, 6, 8, 10-12, and 16-18 comprise millions upon millions of different sequences, the ability of a probe within the set of Hyldig-Nielsen to hybridize to one of the chromosomes listed in the claim is considered a property of the teachings of Hyldig Nielsen and therefore meets the limitation of "detecting, identifying or enumerating chromosomes X, Y, 1-3, 6, 8, 10-12, 16-17 and/or 18".

Conclusion

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. No claims are allowable. It is noted that claim 12 is free of the cited art and 112/1st paragraph rejections. Such claim, however, encompasses nonelected compositions and is thus objected to.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Sitton whose telephone number is (703) 308-6565. The examiner can normally be reached Monday-Thursday from 8:00 AM to 5:00 PM and on alternate Fridays.

Note: The examiner's name has changed from Jehanne Souaya to Jehanne Sitton. All future correspondence to the examiner should reflect the change in name. It is also noted that after January 12, 2004, the examiner will be located at the new USPTO campus and will be reachable at telephone number (571) 272-0752.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 872-9306.

Art Unit: 1634

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jehanne (Souaya) Sitton
Primary Examiner
Art Unit 1634

Jehanne Sitton
1/5/04